REMARKS

The Final Office Action of April 22, 2003, has been received and reviewed. Claims 1-39 are pending in the application. Claims 1-22, 24 and 27-39 stand rejected and claims 23, 25 and 26 have been withdrawn from consideration. Applicants propose to amend claims 1, 2, 6, 9-11, 13-22, 24, 27-30 and 33-37, have canceled claims 3-5, 7, 8, 12, 38 and 39, and propose to add new claims 40-43 as set forth herein. All amendments and cancellations are made without prejudice or disclaimer. Reconsideration is respectfully requested.

Applicants would like to thank the Examiner and his supervisor for the courtesy extended during the interview of August 11, 2003.

Rejections under 35 U.S.C. § 112, second paragraph

Claims 1-22, 24 and 27-39 stand rejected under 35 U.S.C. § 112, second paragraph, as assertedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention. Claims 3-5, 7, 8, 12, 38 and 39 have been canceled rendering the rejections thereof moot. Applicants respectfully traverse the rejections.

Specifically, it was thought that the phrases "first conditions" and "second conditions" in claims 1 and 38 were indefinite. Although applicants do not agree that claims 1 and 38 are indefinite, for the sake of expedited prosecution, applicants have canceled claim 38 and propose to amend claim 1 as set forth herein. As discussed in the interview of August 11, 2003, the phrases "first conditions" and "second conditions" are to be removed from claim 1 and the elements of claim 8 are to be added. Thus, claim 1 should be definite.

With regard to claims 12 and 33-36, it was thought that the recitations of "first pH," "first ion strength" and "second pH" were improper. Claim 12 has been canceled. With regard to the remaining claims, although applicants do not agree that the claims are indefinite, applicants propose to amend the dependent claims to correspond with the proposed amendments to claim 1. Thus, as proposed to amended, the claims should be definite.

Reconsideration and withdrawal of the indefinite rejections are requested.

Rejections under 35 U.S.C. § 112, first paragraph

Claims 1-22, 24 and 27-39 stand rejected under 35 U.S.C. § 112, first paragraph, as assertedly lacking enablement for an antibody or fragment thereof and compositions comprising a binding means that binds to an epitope and is broken from the epitope under any broadly recited conditions. Claims 3-5, 7, 8, 12, 38 and 39 have been canceled rendering the rejections thereof moot. Applicants respectfully traverse the rejections, at least partially, in view of the proposed amendments.

Specifically, it was thought that the applicants have not provided sufficient guidance to enable one skilled in the art to use an antibody or fragment thereof of claim 1 that binds to an epitope and is broken from an epitope under any broadly recited conditions other than those of Table 1. (*See*, Final Office Action, mailed April 22, 2003, page 3). Although applicants do not agree that claim 1 is not enabled, to expedite prosecution of the application, applicants propose to amend claim 1 to include the elements of claim 8 as discussed at the interview.

"It is well settled that patent applicants are not required to disclose every species encompassed by the claims, even in an unpredictable art." (*In re Vaeck*, 947 F.2d 488, 496, 20 USPQ2d 1438, 1450 (Fed. Cir. 1991). Since the specification discloses working examples of antibodies encompassed by claim 1, *i.e.*, table 1 of the specification discloses antibodies that bind to an epitope at a pH of between about 6 and 8 and where the bond between the antibodies and the epitope are broken at a pH within a range of between about 4 and 6 or another range of between about 8 and 8.5, one of ordinary skill in the art would be able to make and use the claimed antibodies without undue experimentation. (*See*, Specification, Table 1, page 7). Accordingly, amended claim 1 is enabled.

Regarding the claims depending from claim 1, they were thought to lack enablement since it was asserted to be unknown how mutually exclusive endpoints can be achieved at the same pH and ion strength. Although applicants do not agree that the claims are not enabled, as proposed to be amended claim 1 recites in part "the selected monoclonal antibody, or fragment thereof, has been selected for its ability to bind to an epitope at a first pH of between about 6 and 8," wherein "the bond of the selected monoclonal antibody, or fragment thereof, to the epitope is broken at a second pH within a range of between about 4 and 6 or another range of between

about 8 and 8.5." Thus, the first pH at which the selected monoclonal antibody of clams 1 binds the epitope is different than the second pH at which the bond between the antibody and the epitope is broken such that mutually exclusive endpoints are not achieved at the same pH.

Regarding the ionic strength, claim 10 requires that the first ion strength at which the selected monoclonal antibody binds the epitope is different than the second ion strength at which the bond between the selected monoclonal antibody and the epitope is broken. Thus, mutually exclusive endpoints are not achieved at the same ion strength.

Accordingly, reconsideration and withdrawal of the enablement rejections are requested.

Rejections under 35 U.S.C. § 102(b)

Claims 1-4, 6-22 and 28-39 stand rejected under 35 U.S.C. § 102(b) as assertedly being anticipated by Beggs et al. as evidenced by Goding. Claims 1-4, 6-21, 24, 27, 28 and 30-39 stand rejected under 35 U.S.C. § 102(b) as assertedly being anticipated by Cummins et al. as evidenced by Goding. Claims 3-5, 7, 8, 12, 38 and 39 have been canceled rendering the rejections thereof moot. Applicants respectfully traverse the rejections as hereinafter set forth.

Neither Beggs et al. nor Cummins et al. discloses all the elements of claim 1 as proposed to be amended. For instance, neither Beggs et al. nor Cummins et al. discloses the binding of an antibody to an epitope at a first pH of between about 6 and 8 and, further, does not disclose the bond between the antibody and the epitope being broken at a second pH of between about 4 and 6 or another range of between about 8 and 8.5. Thus, since neither Beggs et al. nor Cummins et al. discloses each and every element of claim 1, it cannot be anticipated.

The Office Action asserted that Goding stands for the preposition that Beggs et al. and Cummins et al. inherently disclose that an antibody binds to an epitope under first conditions and wherein the bond between the epitope and the antibody is broken under second conditions. (*See*, Final Office Action, mailed April 22, 2003, page 4 and 6). The doctrine of inherency cannot be established for the recited conditions of the antibody of claim 1. As stated by the Federal Circuit, "[u]nder the principles of inherency, if the prior art necessarily functions in accordance with, or includes, the claimed limitations, it anticipates." (*MEHL/Biophile Int'l Corp. v. Milgraum*, 192 F.3d 1362, 1365, 52 USPQ2d 1303, 1305 (Fed. Cir. 1999)). However, "[i]nherency ... may not

be established by probabilities or possibilities. The mere fact that a certain thing *may* result from a given set of circumstances is not sufficient." (*Continental Can Co. USA v. Monsanto Co.*, 948 F.2d 1264, 1269. 20 USPQ2d 1746, 1751 (Fed. Cir. 1991) (emphasis in original)). Since Goding does not establish that the antibodies of Beggs et al. or Cummings et al. necessarily function in accordance with the elements of claim 1, inherency cannot be established.

Goding cannot establish that the antibodies of Beggs et al. or Cummins et al. inherently anticipate claim 1 for the following reasons. First, Goding is a general reference that discusses the characteristics of antibodies generally and does not specifically refer to the antibodies of Beggs et al. or Cummins et al.

Second, Goding discloses that the binding of "some monoclonal antibodies [to their epitope] **may be** very susceptible to minor changes" and does not establish that the antibodies of Beggs et al. or Cummins et al. necessarily function in accordance with the antibodies claim 1. (Goding, pages 44-45) (Emphasis added). Further, Goding was published in 1983 (*See*, Notice of References Cited, part of Paper No. 12) and predates phage display technology as discussed at the interview and disclosed in the specification. As stated in the specification, the monoclonal antibodies were "selected using the per se known 'phage-display' technique." (*See*, Specification, as-filed, page 2).

Further, the specification discloses that only 16 clones out of the entire phage display library, which includes, at the very least, millions of candidate monoclonal antibodies, possess the characteristics of the selected monoclonal antibodies of claim 1 (*See*, *Id.* at page 11) is evidence that the antibodies of Beggs et al. or Cummins et al. would not necessarily share the binding and disassociation properties of the antibodies of claim 1 as required by doctrine of inherency. (*See*, Schering Corp. v. Geneva Pharmaceuticals, Inc., 2003 U.S. App. LEXIS 15496, at *8 (Fed. Cir. 2003).

With further regard to claim 37, it recites that the epitope that the selected antibody of claim 1 binds to is of a *Staphylococcus epidermidis* origin. Since neither Beggs et al. nor Cummins et al. disclose an antibody that binds to an epitope of *Staphylococcus epidermidis* origin, claim 37 cannot be anticipated.

Accordingly, reconsideration and withdrawal of the anticipation rejections are requested.

Rejections under 35 U.S.C. § 103(a)

Claims 1-22 and 28-39

Claims 1-22 and 28-39 stand rejected under 35 U.S.C. § 103(a) as assertedly being unpatentable over Beggs et al. in view of Goding. Claims 3-5, 7, 8, 12, 38 and 39 have been canceled rendering the rejections thereof moot. Applicants respectfully traverse the rejections as hereinafter set forth.

A *prima facie* case of obviousness cannot be established since the cited references do not, alone or in combination, teach or suggest each and every element of independent claim 1 as proposed to be amended. Neither Beggs et al. nor Goding, alone or in combination, teach or suggest an antibody that binds to an epitope at a first pH of between about 6 and 8 or where the bond is broken at a second pH of between about 4 and 6 or another range of between about 8 and 8.5 as recited in claim 1.

Further, no suggestion or motivation exists to combine the cited references. The Final Office Action indicates "it would have been obvious to one of ordinary skill in the art at the time the invention was made to determine all operable and optimal ranges of pH and ion strength at which antibody or fragment thereof binds to and elates from an epitope, as taught by Goding, and use it for antibody or fragment thereof taught by Beggs et al." (Final Office Action at page 8). However, "the mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination." (M.P.E.P. § 2143.01, *citing In re Mills*, 916 F.2d 680, 16 USPQ2d 1430 (Fed. Cir. 1990) (Emphasis in original)).

Beggs et al. does not even recognize the existence of the problem solved by the antibodies of claim 1. As stated in the specification as a drawback of existing antibodies, "the antibody/epitope binding [of antibodies or fragments thereof for detecting dental plaque] is not easily broken." (Specification, page 2, lines 1-4). In fact, Beggs et al. does not even mention the disassociation of the antibody from the epitope. Thus, no suggestion or motivation exists to combine Beggs et al. with Goding.

Rather, the proposed modification of the antibody of Beggs et al. would render the antibody of Beggs et al. unsatisfactory for its intended purpose. "If the proposed modification

would render the prior art invention being modified unsatisfactory for its intended purpose, then there is no suggestion or motivation to make the proposed modification." (M.P.E.P. § 2143.01 *citing*, *In re Gordon*, 733 F.2d 900, 221 USPQ 1125 (Fed. Cir. 1984)). The antibody of Beggs et al. is to be used to bind "a target site, and provides for a therapeutic agent to be connected onto the antibody fragment." (U.S. Pat. 5,490,988, Col. 1, lines 59-61). In Beggs et al., the therapeutic agent may include "oxygen generators or acid producers which could act to modify the environment in the vicinity of a target site. A particular possibility arises if the target site is in the periodontal pocket. Generating oxygen or reducing pH in this cavity would give conditions less favourable for the anaerobic organisms which can invade this pocket." (*Id.* at Col. 4, lines 59-65). Thus, since the antibody of Beggs et al. is used to generate oxygen or **reduce pH** in the periodontal cavity, it stands to reason that it would be undesirable to modify the antibody of Beggs et al. such that the bond between the antibody and the epitope is broken at the lowered pH.

Since a *prima facie* case of obviousness cannot be established, reconsideration and withdrawal of the obviousness rejections over Beggs et al. in view of Goding are, thus, requested.

Claims 1-21, 24, 27, 28 and 30-39

Claims 1-21, 24, 27, 28 and 30-39 stand rejected under 35 U.S.C. § 103(a) as assertedly being unpatentable over Cummins et al. in view of Goding. Claims 3-7, 7, 8, 12, 38 and 39 have been canceled rendering the rejections thereof moot. Applicants respectfully traverse the rejections as hereinafter set forth.

A *prima facie* case of obviousness cannot be established since the cited references do not teach or suggest each and every element of independent claim 1 as proposed to be amended. Cummins et al. and Goding do not, alone or in combination, teach or suggest an antibody that binds to an epitope at a first pH of between about 6 and 8 or where the bond is broken at a second pH of between a range of about 4 and 6 or another range of between about 8 and 8.5.

Further, no suggestion or motivation exists to combine the cited references. The Final Office Action indicates "it would have been obvious to one of ordinary skill in the art at the time the invention was made to determine all operable and optimal ranges of pH and ion strength at

which antibody or fragment thereof binds to and eluted from an epitope, as taught by Goding and use it for antibody or fragment thereof taught by Cummins et al." (Final Office Action at page 10). However, Cummins et al. does not even recognize the problem of eluting the antibody from the epitope since Cummins et al. does not even disclose conditions that break the bond between the antibody and the epitope.

Further, following the reasoning of the Final Office Action that "Weir ed. (Immunochemistry, Volume 1, 1986, p38.1-38.15 Blackwell Scientific Publication, Oxford) teaches that ability of antibody and fragment thereof to bind to and elute from an epitope is unpredictable and varies depending on pH and ion strength" (Final Office Action at page 3), one of ordinary skill in the art would not expect that the antibodies of Cummins et al. could be modified to arrive at the antibody of claim 1. "If the technology is unpredictable, it is less likely that structurally similar species will render a claimed species obvious because it may not be reasonable to infer that they would share similar properties." (M.P.E.P. § 2144.08(e) *citing In re May*, 574 F.2d 1082, 1094, 197 USPQ 601, 611 (CCPA 1978). Accordingly, one of ordinary skill in the art would not expect the antibodies of Cummins et al. to bind to an epitope at a pH of 7 and dissociate from the epitope at a range of between about 4 and 6 or another range of between about 8 and 8.5 as required by independent claim 1, especially when only 16 selected monoclonal antibodies out of millions of antibodies were produced by the applicants.

Accordingly, reconsideration and withdrawal of the obviousness rejections of the claims over Cummins et al. in view of Goding is requested.

Claim 29

Claim 29 stands rejected under 35 U.S.C. § 103(a) as assertedly being unpatentable over Beggs et al. in view of Goding as applied to claims 1-22 and 28-29 above, and further in view of Cole et al. Applicants respectfully traverse the rejections as hereinafter set forth.

Claim 29 is non-obvious, at the very least, as indirectly depending from non-obvious independent claim 1. "If an independent claim is nonobvious under 35 U.S.C. 103, then any

claim depending therefrom is nonobvious." (*In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)).

Reconsideration and withdrawal of the obviousness rejection of claim 29 are, thus, requested.

ENTRY OF AMENDMENTS

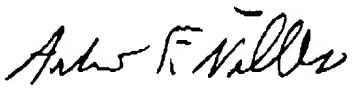
The proposed amendments to claims 1, 2, 6, 9-11, 13-22, 24, 27-30 and 33-37 should be entered by the Examiner because the amendments are supported by the as-filed specification and drawings, and do not add any new matter to the application. Further, the amendments do not raise new issues or require a further search since the added elements were present in the dependent claims. The proposed amendments should also place the application in condition for allowance since they should overcome the rejections of record. Also, the proposed amendments to independent claim 1 should be entered since they adopt suggestions of the Examiner's supervisor presented during the interview. Finally, if the Examiner determines that the amendments do not place the application in condition for allowance, entry is respectfully requested since they certainly remove issues for appeal.

With regard to new independent claim 40 and claims 41-43 depending therefrom, they should be entered since a corresponding number of claims have been canceled and a new search should not be required. For instance, canceled claim 38 was independent and more than three dependent claims were canceled. Further, new claim 40 should be allowable since the recited conditions correspond to working examples as recited in Table 1 of the as filed specification and should be free from the cited references. (*See*, Specification, Table 1, page 7).

CONCLUSION

In view of the proposed amendments and remarks presented herein, applicants respectfully submit that the claims define patentable subject matter. If questions should remain after consideration of the foregoing, the Examiner is kindly requested to contact applicants' attorney at the address or telephone number given herein.

Respectfully submitted,



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